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Original Article

Hemothorax in a Medical Intensive Care Unit: Incidence, Comorbidity and Prognostic Factors

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Background/Purpose: There is a lack of data regarding the occurrence of hemothorax in medical intensive care units (ICUs). The purpose of this study was to investigate the incidence, comorbidity and prognostic factors of hemothorax in medical ICU patients.

Methods: From January 1997 to December 2004, patients with hemothorax that developed during an ICU stay were studied. Hemothorax was considered procedure-related if it developed within 24 hours after an invasive procedure. Medical records were reviewed and analyzed with respect to patients' demographic data, underlying diseases, reasons for admission, Acute Physiology and Chronic Health Evaluation II score, procedures related to hemothorax, management, duration of ICU stay, and outcomes.

Results: Fifty-three patients (0.79%) suffered hemothorax during their ICU stay. Chronic kidney disease (77.4%) was the most common comorbidity. A total of 40 cases (75.5%) were procedure-related. Thoracentesis and chest tube thoracostomy were the most common procedures. The 28-day mortality rate was 35.8%. Multivariate logistic regression analysis revealed that a prothrombin time/international normalized ratio ≥ 1.6 (odds ratio = 10.99, 95% confidence interval = 1.08–112.05) and a hemoglobin decrease ≥ 3 g/dL (odds ratio = 5.55, 95% confidence interval = 1.26–24.45) were significantly associated with 28-day mortality.

Conclusion: Chronic kidney disease was the most common comorbidity associated with hemothorax. Patients with chronic kidney disease might require close observation for hemothorax after invasive procedures, such as thoracentesis and chest tube thoracostomy. Prolonged prothrombin time and decreased hemoglobin level might be of prognostic value for critically ill patients with hemothorax.

Key Words: hemothorax, critical care, prothrombin time, prognostic factor

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In a previous study, hemothorax was found in approximately 50% of patients with blunt chest trauma.[1] However, the incidence of hemothorax in the intensive care unit (ICU) remains unclear. Hemothorax has been reported in 1.0–3.4% of critically ill patients with pleural effusion.[2] In another 1-year study in a medical ICU, four of 1351 patients had hemothorax.[3] The occurrence of hemothorax might be underestimated, given that, in a further previous study, only 82 of 113 patients with pleural effusion underwent thoracentesis.[4]

The etiology of hemothorax in the ICU can be either iatrogenic or spontaneous. The major causes of hemothorax encountered in a medical ICU are venous bleeding as a complication of thoracentesis, pleural biopsy, chest tube placement, or central venous catheterization.[4–6] In contrast, spontaneous hemothorax is uncommon. In some patients, no definite etiology of hemothorax can be determined despite exploratory thoracostomy.[7] Some studies have reported associated morbidity such as malignant pleural disease, and anticoagulation therapy in patients with spontaneous hemothorax.[8,9] There are a paucity of data regarding this condition; hence, the causes of spontaneous hemothorax in the ICU warrant further investigation.

The occurrence of hemothorax in a medical ICU setting has been seldom studied. In addition, little is known about the mortality rate and prognostic factors for hemothorax in critically ill patients. Therefore, in this study we investigated the incidence, etiology, comorbidity, and outcomes of hemothorax in a medical ICU.

Materials and Methods

Patients

From January 1997 to December 2004, patients with a diagnosis of hemothorax who were admitted to the 18-bed medical ICU of National Taiwan University Hospital, Taipei, Taiwan (a 1500-bed tertiary medical center) were eligible for inclusion. The patients were identified from a computer registration database according to the coding system of the International Classification of Diseases, 9th Revision. The diagnosis of hemothorax required that the following criteria were met: pleural effusion with a hematocrit > 50% of that of the circulating hematocrit, or bloody pleural effusion accompanied by a decrease in hemoglobin ≥ 1 g/dL within 24 hours, without other sources of bleeding. Patients were excluded if hemothorax was diagnosed before ICU admission, or if the occurrence of hemothorax was established after chest injury or thoracic/cardiovascular surgery. The Institutional Review Board of National Taiwan University Hospital approved this study. The requirement for informed consent was waived by the review board.

Hemothorax was considered procedure-related if it occurred within 24 hours after the patient had undergone any invasive procedure in the ICU; otherwise, the etiology of hemothorax was considered spontaneous. Medical records were analyzed for age, sex, underlying diseases, reason for ICU admission, Acute Physiology and Chronic Health Evaluation (APACHE) II score,[10] platelet count, the last value of prothrombin time [including the international normalized ratio (INR) and activated partial thromboplastin time] before hemothorax occurred, occurrence of shock, volume of blood components and coagulation factors received by transfusion, invasive procedures performed before the occurrence of hemothorax (including thoracentesis, chest tube thoracostomy, central venous catheterization, pulmonary artery catheterization, pericardiocentesis, and transthoracic lung biopsy), management (including number and duration of chest tube placements), surgical intervention, duration of ICU and hospital stay, and patient outcome.

For the associated morbidity, heart disease included heart failure, arrhythmia, and coronary artery disease. Lung disease included chronic obstructive pulmonary disease and pneumonia. Chronic kidney disease was defined by signs of kidney damage or kidney function impairment for at least 3 months according to the National Kidney Foundation guidelines (Kidney Dialysis Outcomes Quality Initiative). Liver disease included hepatitis and liver cirrhosis. Malignancies

included solid tumors and hematological malignancy. Autoimmune disease was defined as any disorder caused by reactivity with immune system components.

Coagulopathy was defined as abnormal prothrombin time with prolonged INR. The INR was calculated from the patient's prothrombin time and the international sensitivity index value. Prolonged INR was defined as ≥ 1.2 times control. A diagnosis of thrombocytopenia was based on a fall in the platelet count to < 150,000/μL. The amount of blood components transfused immediately during the 72-hour period following the diagnosis of hemothorax was measured, and included whole blood, packed red blood cells, pooled platelets, fresh frozen plasma, and cryoprecipitate.

APACHE II scores were calculated using the clinical data available during the first 24 hours of ICU stay. The reasons for ICU admission were defined as the main problem that necessitated admission. Hypovolemic shock was defined by signs of poor perfusion, with a loss of at least 30% of total blood volume, systolic blood pressure < 90 mmHg, and the requirement for increasing intravascular fluid supply or blood transfusion. Surgical intervention for hemothorax was indicated at our medical ICU if any one of the following conditions existed: > 1 L of blood was evacuated immediately after tube thoracostomy; bleeding from the chest continued at a rate of 150–200 mL/hr for 2–4 hours, or a persistent blood transfusion was required to maintain hemodynamic stability.

Statistical analysis

Continuous variables are expressed as the mean ± standard deviation, whereas categorical variables are expressed as percentages. Quantitative variables were compared using independent samples *t* test, whereas categorical variables were compared using a χ^2 test. A p value < 0.05 was considered statistically significant. Multivariate logistic regression analysis was performed for variables if p was < 0.05. Statistical calculations were performed using SPSS version 14.0 (SPSS Inc., Chicago, IL, USA).

Results

Patient characteristics

There were a total of 6746 admissions to our medical ICU from January 1997 to December 2004. A diagnosis of hemothorax was made in 77 of these patients. Ten patients who had hemothorax related to chest trauma and 14 who had hemothorax as a complication of thoracic/cardiovascular surgery were excluded. Thus 53 patients (0.79%) were included. The demographic characteristics of these patients are summarized in Table 1. Nineteen patients were taking anticoagulation or undergoing antiplatelet therapy. Chronic kidney disease was the most common comorbidity (n = 41, 77.4%), and 16 of these patients required dialysis. The reasons for admission to the ICU are listed in Table 1. Most patients were admitted due to sepsis/septic shock.

Etiology

There were 40 patients with procedure-related hemothorax. Among these, 33 (82.5%) had chronic kidney disease. Fourteen patients were receiving

Table 1. Clinical characteristics of 53 critically ill patients with hemothorax*

Parameters	
Age (yr)	67.8 ± 15.7
Sex, male	29 (54.7)
Underlying conditions	
Chronic renal disease	41 (77.4)
Heart disease	18 (34.0)
Liver disease	16 (30.2)
Lung disease	13 (24.5)
Diabetes	13 (24.5)
Malignancy	10 (18.9)
Autoimmune disease	3 (5.7)
Reasons for admission to ICU	
Sepsis/septic shock	24
Pneumonia/respiratory failure	21
Heart failure	7
Consciousness disturbance	1
Procedure-related	40 (75.5)

**Data presented as mean ± standard deviation or n (%). ICU = Intensive care unit.*

antiplatelet therapy while these procedures were being performed. Thoracentesis ($n=20$) and chest tube thoracostomy ($n=13$) were the most common associated procedures. There were 3233 thoracenteses and 592 chest tube thoracostomies performed in our medical ICU between 1997 and 2004. The overall complication rates of hemothorax because of thoracentesis and chest tube thoracostomy were 0.6% and 2.2%, respectively (Table 2).

There were 13 patients with a diagnosis of spontaneous hemothorax (Table 3). Three of these had coagulopathy, and eight had both coagulopathy and thrombocytopenia. Seven patients had chronic kidney disease, and five had liver cirrhosis. Five patients (cases 2, 4, 5, 9 and 13) were receiving antiplatelet therapy when hemothorax developed. Two patients had malignancies: one with lung cancer (case 4) and one with acute leukemia (case 6).

Table 2. Procedures related to hemothorax in a medical intensive care unit

Procedure	Total	Overall complication (%)
Thoracentesis	3233	20 (0.6)
Chest tube thoracotomy	592	13 (2.2)
Central venous catheterization*	4534	4 (0.1)
Pericardiocentesis	35	2 (5.7)
Percutaneous transhepatic cholangiogram with drainage	91	1 (1.1)

**Including internal jugular venous catheterization, subclavian venous catheterization, and pulmonary artery catheterization.*

Treatment and outcome

Clinical courses and outcomes are summarized in Table 4. A total of 19 patients (35.8%) died within 28 days. Among these, 10 expired due to hypovolemic shock related to hemothorax, and the remaining nine died due to septic shock. For patients with procedure-related hemothorax ($n=40$), 28 received tube thoracostomy and two underwent video-assisted thoracic surgery. The 28-day mortality rate for patients with procedure-related hemothorax was 35.0% ($n=14$). For patients with spontaneous hemothorax ($n=13$), eight received tube thoracostomy and three patients underwent video-assisted thoracic surgery. The 28-day mortality rate for patients with spontaneous hemothorax was 38.5% ($n=5$).

Patient characteristics and management were analyzed for possible prognostic factors of iatrogenic and spontaneous hemothorax. There was no

Table 3. Characteristics of 13 patients with spontaneous hemothorax

Case	Age (yr)/sex	Comorbidity	Hb decrease (g/dL)	Platelet (/μL)	PT (INR)	Cr (mg/dL)	Management	28-day outcome
1	66/M	CRD	4.3	74	1.42	2.90	VATS	Death
2	93/M	Sick sinus syndrome	1.3	196	1.11	1.00	SC	Death
3	76/F	ESRD	0.5	148	1.53	3.80	CTT	Death
4	71/F	Lung cancer	3.9	66	1.28	0.88	CTT	Death
5	61/M	CRD; liver cirrhosis	4.1	171	1.66	0.89	CTT	Death
6	27/M	Leukemia	2.3	34	1.20	2.60	VATS	Survival
7	60/M	CRD; liver cirrhosis	1.0	38	1.57	3.10	CTT	Survival
8	49/M	CRD; liver cirrhosis	2.3	48	1.26	3.00	SC	Survival
9	87/F	CRD	1.1	377	1.16	1.46	SC	Survival
10	51/M	ESRD; liver cirrhosis	3.0	63	1.53	7.30	CTT	Survival
11	45/M	Pulmonary tuberculosis	0.3	17	1.50	0.80	VATS	Survival
12	42/M	Liver cirrhosis	0.5	115	3.13	2.60	CTT	Survival
13	72/F	Coronary artery disease	1.2	359	1.25	0.80	CTT	Survival

M = Male; F = female; Hb = hemoglobin; PT = prothrombin time; INR = international normalized ratio; Cr = creatinine; CRD = chronic renal disease; ESRD = end-stage renal disease; VATS = video-assisted thoracoscopic surgery. CTT = chest tube thoracostomy; SC = supportive care.

Table 4. Clinical features and outcomes of 53 critically ill patients with hemothorax

Clinical features and courses	Survival ($n=20$)	Non-survival ($n=33$)	p
APACHE II score	28.4 ± 5.3	27.4 ± 4.8	0.517
White cell count (/μL)	12,145.3 ± 7407.9	15,005.8 ± 10,901.5	0.315
Hemoglobulin (g/dL)	8.4 ± 1.7	8.0 ± 2.4	0.457
Platelet count (/μL)	135.3 ± 93.9	120.2 ± 114.7	0.605
Prothrombin time (sec)	15.7 ± 6.3	22.7 ± 17.4	0.141
Creatinine (mg/dL)	2.5 ± 2.5	1.9 ± 1.4	0.258
Aspartate aminotransferase (U/L)	52.7 ± 19.6	51.4 ± 33.8	0.906
Decrease of hemoglobin (g/dL)	2.36 ± 1.77	3.53 ± 1.53	0.019
Decrease of platelet count (/μL)	37.9 ± 36.8	55.3 ± 53.9	0.279
International normalized ratio	1.33 ± 0.41	2.16 ± 1.76	0.018
Management			
CTT with drainage	11 (55.0)	24 (72.7)	
Thoracentesis with drainage	4 (20.0)	4 (12.1)	
VATS	2 (10.0)	3 (9.1)	
Conservative treatment and/or blood component therapy	3 (15.0)	2 (6.1)	
Outcome			
ICU stay (d)	37.1 ± 37.1	26.9 ± 26.9	0.253
Hospital stay (d)	80.4 ± 56.8	43.8 ± 40.6	0.008

APACHE II = Acute Physiology and Chronic Health Evaluation II; CTT = chest tube thoracostomy; VATS = video-assisted thoracoscopic surgery; ICU = intensive care unit.

significant difference in either mortality rate or prognostic factors between these two subgroups.

Prognostic factors

We investigated the differences in clinical features between the survival and non-survival groups. The survival group had lower INR levels (survival *vs.* non-survival = 1.33 ± 0.41 *vs.* 2.16 ± 1.76, $p = 0.018$) and a less pronounced hemoglobin decrease (survival *vs.* non-survival = 2.36 ± 1.77 g/dL *vs.* 3.53 ± 1.53 g/dL, $p = 0.019$). There were no statistically significant differences between the survival and non-survival groups for the other variables, including age, sex, APACHE II score, reason for admission, comorbidity, etiology (spontaneous *vs.* iatrogenic), partial thromboplastin time, platelet count, albumin level, blood urea nitrogen, creatinine, and type of management.

Multivariate analysis revealed that prothrombin time INR ≥ 1.6 [$p = 0.043$, odds ratio (OR) = 10.99, 95% confidence interval (CI) = 1.08–112.05] and hemoglobin decrease ≥ 3 g/dL ($p = 0.024$, OR = 5.55, 95% CI = 1.26–24.45) were significantly associated with 28-day mortality (Table 5). With each 1-g/dL decrease in hemoglobin, the relative risk of 28-day mortality increased by 55.4%. If the INR level increased by 0.1 from 1.0, the relative risk of 28-day mortality increased by 32.2%.

Discussion

In this study, we demonstrated that the incidence of hemothorax in a medical ICU was 0.79%. Chronic kidney disease was the most common associated morbidity. Most cases of hemothorax were procedure-related, with thoracentesis and chest tube thoracostomy being the most common related procedures. The prothrombin time

Table 5. Variables that significantly influenced the 28-day mortality of 53 critically ill patients with hemothorax

Variable	Number of patients		Multivariate analysis
	Total	Number of death (%)	OR (95% CI)
Prothrombin time INR			
< 1.6	45	12 (26.7)	1
≥ 1.6	8	7 (87.5)	10.99 (1.08–112.05)
Hemoglobin decrease (g/dL)			
< 3	31	6 (19.4)	1
≥ 3	22	13 (59.1)	5.55 (1.26–24.45)

INR = International normalized ratio; OR = odds ratio; CI = confidence interval.

INR and the level of hemoglobin decrease were identified as potential prognostic factors.

Thoracentesis has traditionally been performed widely in the ICU for patients with pleural effusion. Doyle et al reported that only two patients developed hemothorax after 174 thoracentesis procedures in 110 patients.[11] Bass et al identified only two cases of hemothorax out of a total of 100 thoracentesis procedures performed in 100 patients with hematologic malignancies.[12] In a 1-year study in which 1640 patients were admitted to the medical ICU, 118 thoracenteses were performed in 94 febrile patients, with hemothorax occurring in two of these.[13] In the same study, the complication rate of hemothorax that resulted from thoracentesis was 0.6%.

In our ICU, transthoracic sonography was performed routinely before thoracentesis to estimate pleural effusion volume. Guidance by transthoracic sonography might be useful to decrease the incidence of hemothorax associated with thoracentesis. Prior studies reported incidences of hemothorax complicating tube thoracostomy of 3–36% in the ICU.[14,15] Etoch et al analyzed factors related to complications during this procedure in a single trauma center.[16] They have reported that 379 patients required 599 tube thoracotomies, with hemothorax occurring as a complication in 16 of these patients.[16]

Tube thoracostomy is associated with significant morbidity. It has been reported that differences in complication rates vary between physicians, which suggests that additional training is indicated in some instances.[17] In our medical ICU, tube thoracostomy was performed by senior physicians with the aid of transthoracic sonography. There were 13 cases of hemothorax (2.2%) which resulted from complications of 592 chest tube thoracostomies. Tube thoracostomy performed after sonographic evaluation to determine the location and amount of pleural effusion might be helpful to decrease the occurrence of hemothorax.

Chronic kidney disease was the most common comorbidity in our study. Uremic patients are known to suffer bleeding diathesis due to platelet dysfunction, with occurrence of pleural hemorrhage after invasive procedures, which has been highlighted in several case reports.[18,19] Vanherweghem et al reviewed the complications related to subclavian catheterization for hemodialysis.[20] In that review, major complications such as pneumothorax and hemothorax that were related to the subclavian route for dialysis occurred in 22 patients who had 1288 catheter insertions. This reflects a 1.7% rate of traumatic complication in patients who are receiving dialysis.[20] McVay et al demonstrated that patients with markedly elevated serum creatinine levels (6.0–14.0 mg/dL) had a significantly greater average decrease in hemoglobin [-0.82 ± 1.3 g/dL ($n = 11$) *vs.* -0.12 ± 0.88 g/dL ($n = 450$), $p = 0.011$], compared with patients who had normal serum creatinine levels (0.4–1.4 mg/dL), after paracentesis and thoracentesis in a group with mild coagulation abnormalities.[21] Uremia-related bleeding diathesis might contribute to iatrogenic hemothorax in the medical

ICU. Therefore, patients with CKD might require close observation for hemothorax after invasive procedures, such as thoracentesis and chest tube thoracostomy.

The occurrence of spontaneous hemothorax is rare. We reported 13 patients with spontaneous hemothorax. Eleven of these were diagnosed with coagulopathy or thrombocytopenia. Five patients (2 with atrial fibrillation, 2 with coronary artery disease and 1 with ischemic stroke) received antiplatelet therapy. Only two patients had active malignancies, however, in these patients, hemothorax was not related to pleural metastasis. Martinez et al described six cases of spontaneous hemothorax and also have reviewed the literature from 1862 to 1991 for additional cases.[17] A total of 18 hemothorax cases have been reported in native coagulopathy, including hemophilia, thrombocytopenia, and von Willebrand disease. Hemothorax occurred in 1.5% of hemophilia cases.[22] Fourteen cases of hemothorax that resulted from complications related to anticoagulation therapy have been reported.[17] There have been four reported cases of malignancies causing hemothorax without invading the pleura (2 rib Ewing sarcomas, 1 lung cancer, and 1 chronic myelocytic leukemia).[17]

In our study, increased prothrombin time INR was significantly associated with 28-day mortality. Prothrombin time has been identified as an independent prognostic factor in previous studies pertaining to major trauma. Murray et al studied 840 patients with traumatic brain injury, from three of the relevant studies within the International Mission for Prognosis and Clinical Trial (IMPACT) database.[23] Prolonged prothrombin time was associated with poor prognosis (OR = 1.64, 95% CI = 1.34–2.00). Kawai et al analyzed abnormalities in preoperative laboratory data in 101 patients who underwent surgery for colorectal perforations.[24] Prolonged prothrombin time (survivors *vs*. non-survivors = 84.6 ± 14.9% *vs.* 62.2 ± 17.2) and activated partial thromboplastin time [survivors *vs*. non-survivors = 31.5 ± 7.3 sec *vs.* 47.1 ± 15.8 sec) were significantly correlated with poor prognosis. Among the several risk factors analyzed, the presence of coagulation disorders (prothrombin time < 70% of control or activated partial thromboplastin time > 40 sec) was an independent predictive factor of postoperative mortality. Further investigation to derive the prognostic value of prothrombin time and explore the clinical impact of aggressively correcting coagulation abnormalities might be warranted.

There were several limitations to our study. First, the case number was small and much variation could not be investigated. Second, hemothorax was diagnosed by the analysis of pleural effusion. When pleural effusion was first detected upon physical examination or chest radiography, thoracentesis was performed in accordance with published guidelines.[25–27] Therefore the incidence of hemothorax could have been underestimated. Third, because of the retrospective study design, no standard protocol could be followed with regards to the detection and management of hemothorax.

In conclusion, chronic kidney disease was most commonly associated with hemothorax. Patients with chronic kidney disease might require close observation for hemothorax after invasive procedures, such as thoracentesis and chest tube thoracostomy. Assessment of prothrombin time INR and hemoglobin levels could be of prognostic value in critically ill patients with hemothorax.

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